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METHOD AND COMBINATION ELECTRONIC COMMUNICATION AND MEDICAL DIAGNOSTIC APPARATUS FOR DETECTING/MONITORING NEUROPATHY

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BACKGROUND OF THE INVENTION

[0001] The present invention is generally directed to a medical diagnostic apparatus, and more particularly to a combination electronic communication and medical diagnostic apparatus which can be used as an electronic communication device, such as a beeper/pager or cellular phone, as well as a medical tool to detect and/or monitor neuropathy.

[0002] Diabetes is a very common disease that often leads to painful neuropathy. Symptomatic diabetic neuropathy is preceded by an asymptomatic phase during which nerve conduction by the large fibers is impaired, leading to an impairment of vibration perception. Vibration threshold

is a continuous measure and by necessity, categorization into a binary outcome will mean setting of an arbitrary threshold. The 95th and 97th percentiles in non-diabetic populations have previously been used as thresholds for neuropathy. Vibration threshold is the most valid measure of nerve function in diabetic patients and has been used as a gold standard.

[0003] Vibration testing has long existed in various manners. For example, vibration threshold testing devices are currently being used which include two fixed probes in one or two boxes which are placed on a table or floor. The patient must touch them with the fingers or toes and indicate which one is vibrating. A further vibrating tool known as Biothesiometer, which is similar to vibrating devices sold in adult paraphernalia shops, is applied to an extremity and the vibration level is turned up until the patient can feel the vibration. The level is then read off a meter. These devices have also been computer driven.

[0004] A further example of vibration testing is by the utilization of a tuning fork, which can be applied to an extremity. A vibrating pen for detecting nerve impairment (neuropathy) is disclosed by Laudadio in U.S. Patent No. 5,931,793. However, this is merely a pen-like device that does not incorporate the function of a beeper/pager or cellular phone. Furthermore, Laudadio's pen-like device measures vibration threshold as a binary outcome requiring setting

of arbitrary thresholds used to define the severity of neuropathy as mild, moderate or severe.

[0005] A vibrating pen marketed by Solarwide Inc. sends a signal to indicate that the user has a call on a cellular phone but its use for the detection of neuropathy has not been described. Another form of vibrating pen known as a Wiggle Writer for children is disclosed in U.S. Patent No. 5,208,987, which operates on a similar principle using an offset motor which causes the pen tip to draw circles.

[0006] A quantitative assessment of vibration threshold over a wide range of frequencies using various vibratory amplitude levels at vibration frequency is disclosed by Lacourse and McCoy in U.S. Patent No. 5,002,065, in which they show that an increase in the perception threshold for vibration is the earliest detectable objective sign of carpal tunnel syndrome. Lee et al. have demonstrated the usefulness of determining vibration perception threshold in patients with end-stage renal disease as a measure of neuropathy (*Kidney International*, Vol 64, pp. 1089-1094, 2003). There are several other medical conditions, including alcohol abuse and vitamin deficiencies, that are associated with neuropathy.

[0007] Loss of large myelinated fibres is the most constant morphologic feature of neuropathy in patients with kidney failure or uremia. Impaired vibration perception of the toes is early and initially the only clinical sign of this peripheral neuropathy (G. Said, L. Boudier, J. Silva, J. Zingraff, T. Druecke: Different patterns of uremic polyneuropathy:clinicopathologic study. *Neurology* 33:567-574, 1983) and measurement of vibratory perception thresholds is more suitable to evaluate progression or recovery of uremic neuropathy than is measurement of nerve conduction velocity (Said et al, Id., and FGI Jennekens, EJ Dorhout Mees, D Van der Most van spijk: Uremic polyneuropathy. *Nephron* 8: 414-426, 1971).

[0008] Although vibration threshold has been recognized as the gold standard for diabetic neuropathy, the investigators have been testing alternative measures as surrogates for the diagnosis of neuropathy (Rahman et al., *Diabetic Medicine* 20: 368-374, 2003), because the currently available devices used to determine vibration threshold are cumbersome, mostly used as research tools, and are not widely available in the primary care setting. In fact, majority of physicians, including the inventor of this invention have never seen the vibrameter devices, let alone use it.

[0009] In common clinical practice, the current standard of medical care is to use tuning fork as qualitative, or at best semiquantitative tool, for diagnosing neuropathy. However, tuning forks are cumbersome, inaccurate, operator-dependent and consequently are used infrequently and only by a small minority of physicians. In addition, in using a tuning fork, physicians tend to underestimate or overestimate the loss of vibration sensation. In diabetic patients tuning fork overestimates loss of vibration, compared with quantitative vibration threshold using a vibrameter (TM Burns, A Taly, O'Brien, PJ Dyck: Clinical versus quantitative vibration assessment: improving clinical performance. *Journal of the Peripheral Nervous System* 7:112-117, 2002). On the other hand, in uremic patients, tuning fork examination could demonstrate abnormalities in only 2.5% of patients whereas vibrameter was much more sensitive, detecting abnormalities in 47.5% of patients, similar to the 45% using nerve conduction velocity as the gold standard (MJ Hilz, P Zimmermann, G Rosl, W Scheidler, J braun, B Stemper, B Neundorfer: Acta Neurol Scand. 92(6):486-90, 1995). Similarly, in the same study, in alcoholic patients tuning fork revealed abnormalities in only about 15% compared to 60% by vibrameter and about 35% by nerve conduction velocity. Therefore, it is evident that use of tuning fork is inaccurate and inadequate as a clinical tool for the detection of neuropathy in diabetic, uremic or alcoholic patients. On the other hand, vibrameter is more sensitive and specific for the detection of neuropathy since

it employs quantitative stimuli, a broad range of stimulus magnitudes and null stimuli.

[0010] None of the diagnostic or monitoring devices described above, however, serve as electronic communication devices, either, for example, as a receiving pager or a cellular phone.

[0011] In view of the drawbacks associated with conventional tools and techniques, there is a need for a better and improved clinical tool for the detection and/or monitoring of neuropathy that is portable, can be easily carried by a physician or other health care professional on their person, and is more sensitive and specific compared to the tuning fork.

OBJECTS AND SUMMARY OF THE INVENTION

[0012] The principal object of the present invention is to provide an apparatus and method for detecting and/or monitoring neuropathy which overcomes the drawbacks associated with conventional devices and/or or techniques.

[0013] An object of the present invention is to provide a diagnostic method and apparatus for detecting and/or monitoring nerve impairment or neuropathy.

[0014] Another object of the present invention is to provide an easily portable neuropathy detection and/or monitoring apparatus which is incorporated in an electronic communication device, such as a beeper/pager or cellular phone that the vast majority of medical professionals routinely carry on their person.

[0015] Yet another object of the present invention is to provide a diagnostic apparatus for detecting and/or monitoring neuropathy which also functions as an electronic communication device, such as a beeper/pager or cellular phone.

[0016] Still yet another object of the present invention is to provide a compact and easy to carry apparatus which has the dual functions of electronic communication, such as a beeper/pager or cellular phone, and medical diagnostic tool for detecting and/or monitoring neuropathy. The apparatus allows a health care professional to perform simple and quick, yet accurate test to determine neuropathy in a subject. The apparatus produces instant results allowing the health care professional to refer the subject for

further diagnostic evaluation when the primary cause of neuropathy is not apparent.

[0017] An additional object of the present invention is to provide a combination electronic communication and medical diagnostic apparatus which can be used to detect and/or monitor neuropathy caused by various medical conditions or ailments, such as diabetes, kidney failure or uremia, alcohol abuse, vitamin deficiencies, and carpal tunnel syndrome.

[0018] Yet an additional object of the present invention is to provide a combination electronic communication and medical diagnostic apparatus which can precisely quantitate and audibly or visibly indicate the vibration perception threshold (VPT), vibration disappearance threshold (VDT), and/or vibration threshold (VT), wherein VT is calculated as a composite of VPT and VDT. Quantitative measure of VT allows monitoring the progression of neuropathy over time.

[0019] A further object of the present invention is to provide a combination electronic communication and medical diagnostic apparatus which can be easily used by a person for self-diagnostic or self-evaluation purposes for detecting and/or monitoring neuropathy.

[0020] In summary, the main object of the present invention is to provide a neuropathy detection and/or monitoring apparatus which also functions as an electronic communication device, such as a beeper/pager or cellular phone. The apparatus, in view of its dual functionality, is easy and inexpensive to manufacture, and is further easy to carry by health care professionals who routinely carry beepers/pagers or cellular phones.

[0021] One of the above objects is met, in part, by the present invention which in one aspect includes a combination electronic communication and medical diagnostic apparatus, which comprises a first component for transmitting or receiving a remote communication signal and a second component for generating vibration to be used in a medical diagnosis.

[0022] Another aspect of the present invention includes a combination electronic communication and medical diagnostic apparatus, which comprises a device for generating vibration in first and second modes. One of the first and second modes is utilized in an electronic communication and the other of the first and second modes is utilized in a medical diagnosis.

[0023] Another aspect of the present invention includes an electronic communication apparatus for detecting neuropathy in a subject, which comprises a component for generating vibration of a fixed or variable

magnitude, wherein when the apparatus is applied to a subject, threshold for the perception or disappearance of vibration can be determined as a measure of nerve function to detect neuropathy.

[0024] Another aspect of the present invention includes a medical diagnosis method, which comprises: providing a combination electronic communication and medical diagnostic apparatus, the apparatus including a first component for transmitting or receiving a remote electronic communication signal, and a second component for generating vibration to be used in a medical diagnosis; generating vibration and applying the apparatus to a subject; and diagnosing a medical condition based on detection or non-detection of vibration by the subject.

[0025] Another aspect of the present invention includes a method of detecting neuropathy in a subject, which comprises: providing a combination electronic communication and medical diagnostic apparatus, the apparatus including a first component for transmitting or receiving a remote electronic communication signal, and a second component for generating vibration to be used in detecting neuropathy; generating vibration of a predetermined magnitude or frequency as a threshold stimulus and applying the apparatus to a subject; and allowing the subject to indicate whether or not vibration can be

detected; wherein the absence or presence of neuropathy is indicated by the subject's ability to detect or not detect the vibration.

[0026] Another aspect of the present invention includes a medical diagnostic method, which comprises: providing a combination electronic communication and medical diagnostic apparatus, the apparatus including a first component for transmitting or receiving a remote electronic communication signal, and a second component for generating vibration to be used in a medical diagnosis; applying the apparatus to a subject and generating vibration; and diagnosing a medical condition based on detection or non-detection of vibration by the subject.

[0027] Another aspect of the present invention includes a method of detecting neuropathy in a subject, which comprises: providing a combination electronic communication and medical diagnostic apparatus, the apparatus including a first component for transmitting or receiving a remote electronic communication signal, and a second component for generating vibration to be used in detecting neuropathy; applying the apparatus to a subject and generating vibration of a predetermined magnitude or frequency as a threshold stimulus; and allowing the subject to indicate whether or not vibration can be detected; wherein the absence or presence of neuropathy is indicated by the subject's ability to detect or not detect the vibration.

BRIEF DESCRIPTION OF THE DRAWINGS

[0028] The above and other objects, novel features and advantages of the present invention will become apparent from the following detailed description of the preferred embodiment(s) of the invention, as illustrated in the drawings, in which:

[0029] Figure 1 is a schematic illustration of various components of a combination electronic communication and medical diagnostic apparatus of the present invention;

[0030] Figure 2 illustrates a flow chart of a method of the invention for detecting neuropathy in a subject;

[0031] Figures 3-4 illustrate a flow chart of a method of the invention for determining vibration perception threshold (VPT) and determining and grading the severity of neuropathy in a subject; and

[0032] Figures 5-6 illustrate a flow chart of a method of the invention for determining vibration disappearance threshold (VDT) and determining and grading the severity of neuropathy in a subject.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT(S) OF THE INVENTION

[0033] The present invention is based, at least in part, on the principle of creating a vibration by a small portable device, such as a beeper/pager or cellular phone. The vibrating device itself, or a probe extending from the device, is applied to the patient's extremity (finger, toe, tibia, wrist, face, etc.) and vibrates at a magnitude (or amplitude) and/or frequency which determines a specific level or threshold for the patient's ability to detect vibration. The magnitude, although preferably fixed, can be selected to be low (for minimal detection of threshold impairment), medium (to detect moderate neuropathy) or high (to detect severe neuropathy). If the patient can feel the vibration, set at a pre-selected level, the patient's threshold is lower than the level set. Conversely, if the patient cannot feel the vibration, the patient's threshold is higher than the level set.

[0034] However, vibration threshold is a continuous measure. Therefore, the present invention has been devised to precisely quantitate and display the vibration perception threshold (VPT), vibration disappearance threshold (VDT), and/or vibration threshold (VT) calculated as a composite measure of VPT and VDT. Quantitative measure of vibration threshold allows monitoring the progression of neuropathy over time. Vibration perception

threshold (VPT) is known as the smallest stimulus magnitude (expressed in physical units) that is felt. To determine VPT, the stimulus strength is gradually increased from zero to the point where a vibratory sensation is first perceived. Subsequently, the stimulus strength is diminished from a supraliminal level until the sensation disappears. This indicates vibration disappearance threshold (VDT). Therefore, VDT is the largest stimulus magnitude (expressed in physical units) that is not felt. The average of VPT and VDT is known as the vibration threshold (VT).

[0035] As illustrated schematically in Figure 1, the communication and medical diagnostic apparatus CMD of the present invention includes a motor 10 for generating vibration, which is connected to a vibrating head 12 by a shaft 14. A power source 16, preferably a battery, provides electrical power to the motor 10. A vibration mode selector 18 allows a user to operate the apparatus CMD, either in the communication mode to receive or transmit signals via a communication signal receiver/transmitter 20 for paging, voice, data, etc., purposes, or in the diagnostic mode to detect or monitor neuropathy. In the communication mode, the motor 10 generates vibration at, for example, standard paging or beeping magnitude or frequency. In the diagnostic mode, however, the user can select to generate vibration at a desired magnitude (or amplitude) and/or frequency by activating the magnitude/frequency selector 22. In particular, the apparatus CMD is pre-

programmed to generate vibration of a fixed or variable magnitude and/or frequency. The fixed magnitude would be of various preselected values that can be chosen by the user. Likewise, the variable magnitude would vary at preselected values in a linear, curvilinear, or step-like manner, that can also be chosen by the user. Along the same lines, the apparatus CMD is operable to generate vibration at various preselected fixed or variable frequencies.

[0036] The apparatus CMD is further provided with a display 24 to indicate the selected magnitude and/or frequency of the vibration. In addition to or as an alternative, the apparatus CMD may be provided with a mechanism to audibly indicate the vibration magnitude and/or frequency. Although not shown, the apparatus CMD may include a suitable memory chip and a microprocessor, or the like components for storing and/or processing the data, such as tested VPT, VDT, VT, etc. This would be particularly useful in monitoring the progress of treatment for neuropathy over time and/or to perform serial evaluation in, for example, hemodialysis patients. In addition, this would assist a person in detecting (or monitoring) neuropathy for self-diagnostic or self-evaluation purposes.

[0037] The apparatus CMD can be made of any suitable durable material, including an outer casing of plastic or metal of any color. The casing may contain a barrel, or a barrel within a barrel, to isolate the vibration from

the outer casing. The battery(ies) would preferably be mounted inside a conducting aluminum plated cardboard barrel, which in turn would be mounted inside the outer casing or barrel(s) to provide a complete electrical circuit between an operating switch, battery(ies), and motor, or can be placed directly in the casing and wiring can be used to complete the circuit.

[0038] The vibrating head or probe 12 is preferably made of a plastic or metal material and may have a tubular or solid configuration projecting out from an end of the apparatus CMD.

[0039] The motor 10 can be a small DC motor with an offset weight on the shaft 14, or a piezoelectric or other transducer, capable of generating a vibration of a magnitude and/or frequency that is low enough not to be heard by the subject, but sufficient to allow detection.

[0040] Figures 2-6 illustrate flow charts for carrying out various methods/procedures in accordance with the present invention. In particular, Figure 2 illustrates a method for determining neuropathy in a subject. Figures 3-4 illustrate a method for determining vibration perception threshold (VPT) and determining and grading the severity of neuropathy in a subject. Likewise, Figures 5-6 illustrate a method for determining vibration disappearance threshold (VDT) and determining and grading the severity of neuropathy in a

subject. Any of these procedures may be followed, as appropriate, in the event, a physician or other health care professional in a medical consultation of a subject suspects the presence or onset of a medical condition, ailment or disease that causes neuropathy or nerve impairment, such as diabetes, kidney failure or uremia, alcohol abuse, carpal tunnel syndrome, and/or vitamin deficiencies.

[0041] Referring to Figure 2, after initial consultation (step 10), the subject is further screened for symptoms of neuropathy (step 12). If the medical professional feels that further testing would be beneficial, the subject is then prepared for vibration testing (step 14)). In order to test the subject's ability to detect vibration, the communication and medical diagnostic apparatus CMD of the present invention is set to the diagnostic mode by actuating the vibration mode selector 18, and a preset standard for magnitude or frequency is selected (step 16) by using the magnitude/frequency selector 22. For instance, the preset standard may correspond to the 95^{th} and 97^{th} percentiles in a non-diabetic population as threshold for neuropathy.

[0042] After the apparatus CMD has been set to a desired or preset magnitude or frequency, it is operated to generate vibration (step 18) and applied to an extremity of the subject (step 20). The subject is then asked whether or not he/she can detect the vibration (step 22). The detection of

vibration by the subject would indicate the absence of neuropathy (step 24) and the procedure is ended (step 26). On the other hand, if the vibration is not detected by the subject, this would indicate the presence of neuropathy (step 28) and the procedure is ended (step 30).

[0043] Figures 3-4 illustrate a method for determining vibration perception threshold for a subject. As shown, a subject is initially consulted by a health care professional (step 32) and then screened for symptoms of neuropathy (step 34). The subject is then prepared for vibration testing (step 36) and the apparatus CMD is readied for testing by selecting a magnitude or frequency of vibration by actuating the magnitude/frequency selector 22 (step 38). The apparatus CMD is then operated to generate vibration (step 40) and applied to an extremity of the subject (step 42). The subject is then asked whether or not he/she can detect the vibration (step 44). If the subject cannot detect the vibration, the magnitude or frequency of vibration is gradually increased (step 46) and steps 40, 42 and 44 are repeated until the subject is able to detect the vibration. The value at which the subject is able to detect the vibration would indicate the vibration perception threshold (VPT) for the subject (step 48). In order to confirm the VPT value determined in step 48, or to obtain a more reliable value, the procedure may be repeated (step 50) to obtain several VPT values to obtain an average. The VPT value determined in step 48 is then compared with a preset standard or normal value (step 52).

If the tested VPT (determined in step 48) is normal (step 54), the absence of neuropathy is indicated (step 56) and the procedure is ended. On the other hand, if the tested VPT is higher than normal (step 60), the presence of neuropathy is indicated (step 62). If the presence of neuropathy is indicated (step 62), the severity of neuropathy is graded, for example, low, medium, or high (step 64) based on the difference between the tested VPT and the preset standard. The final diagnosis is then rendered (step 66) and the procedure is ended (step 68).

[0044] Figures 5-6 illustrate a method for determining vibration disappearance threshold for a subject. As shown, a subject is initially consulted by a health care professional (step 70) and then screened for symptoms of neuropathy (step 72). The subject is then prepared for vibration testing (step 74) and a magnitude or frequency of vibration is selected on the apparatus CMD (step 76). The apparatus CMD is then operated to generate vibration (step 78) and applied to an extremity of the subject (step 80). The subject is then asked whether or not he/she can detect the vibration (step 82). If the subject cannot detect the vibration, the magnitude or frequency of vibration is gradually increased (step 84) and steps 78, 80 and 82 are repeated until the subject is able to detect the vibration. Once the subject is able to detect the vibration, the magnitude or frequency is then gradually decreased until the subject can no longer detect vibration (step 86). The value

at which the subject can no longer detect the vibration, indicates the vibration disappearance threshold (VDT) for the subject. In order to confirm or obtain a more reliable VDT value, step 86 may be repeated to obtain several values to obtain an average (step 88). The tested VDT (step 86) is then compared with a preset standard or normal value (step 88). If the tested VDT is normal (step 90), the absence of neuropathy is indicated (step 92) and the procedure is ended (step 94). On the other hand, if the tested VDT is higher than normal (step 96) the presence of neuropathy is indicated (step 98), which is then graded, for example, low, medium, or high (step 100). The final diagnosis is then rendered (step 102) and the procedure is ended (step 104).

[0045] With respect to the above-described procedures, it is noted that the use of preset standard and/or prevalidated algorithms to test and to estimate threshold would greatly facilitate use of vibration testing to diagnose or monitor neuropathy in a clinical setting. These standards and/or algorithms would be created after determination of reference values based on a randomly chosen reference group that is free from neurological disease or disorder, neuropathy, or other diseases predisposed to cause neuropathy. This group would then be tested to determine a threshold value for the magnitude and/or frequency of vibration at which the vibration is normally detected. Based on these values, vibration magnitude and/or frequency would be expressed as

percentiles for determining, monitoring or confirming neuropathy in a subject suspected of having this condition.

[0046] It is noted herewith that while in the methods illustrated in Figures 2-6, the apparatus CMD of the invention is applied to an extremity of the subject after generating vibration, it is within the scope of the invention to generate vibration after applying the apparatus CMD to the subject.

[0047] A standard diagnostic application of the present invention is for the neurodiagnostic assessment of hemodialysis patients for kidney failure. This provides a very sensitive predictor of morbidity and mortality in dialysis patients. Through manual recording or database functioning (i.e., storing and/or processing of test subject data) of the present apparatus, a comparison of measures from one testing period to another is performed in order to assess overall neurological health of an individual with respect to their health condition (i.e., kidney dialysis patient). For example, uremic patients are routinely evaluated every three months. By using this automatic diagnostic feature of the present apparatus, serial measurements from uremic patients may be compared and an estimation of the neurological stability of the patient may be provided as part of the diagnostic output of the present apparatus. Such information would be valuable to a nephrologist in determining whether to maintain the present level of kidney dialysis or increase dialysis dose for the

patient being evaluated. The ability to perform such serial evaluations is an important feature of the present invention.

[0048] Although vibratory testing devices have been available for some time and vibrating pens are known, the present invention represents the first time that a medical device has been proposed that tests for vibration perception and disappearance thresholds utilizing an electronic communication and medical diagnostic apparatus. The usefulness of the invention is apparent considering that billions of dollars are spent each year on diabetic foot problems related to diabetic neuropathy. Yet a device such as of the invention has not yet been proposed. However, if a simple, inexpensive device such as the CMD apparatus of the invention, were available to nurses, physicians, and other health care professionals, neuropathy could be detected early and many ulcers, infections, and amputations might be avoided by instituting proper foot care early. In addition, once detected, the treatment of neuropathy could be easily monitored by using the apparatus CMD of the invention. In addition, since the apparatus CMD could be easily used by a subject for self-diagnostic or self-monitoring purposes, early self-detection and improved monitoring would result leading to reduction in overall health care spending and better well-being for the patients.

[0049] While this invention has been described as having preferred sequences, ranges, steps, materials, structures, features, and/or designs, it is understood that it is capable of further modifications, uses and/or adaptations of the invention following in general the principle of the invention, and including such departures from the present disclosure as those come within the known or customary practice in the art to which the invention pertains, and as may be applied to the central features hereinbefore set forth, and fall within the scope of the invention and of the limits of the appended claims.